REMARKS

Original claims 1-50 are currently pending in this application. Applicants have canceled claims 51-147 without prejudice to the Applicants' right to file one or more continuation, divisional, or continuation-in-part applications. No new matter has been introduced into this application.

Applicants submit herewith a new set of drawings to overcome the Examiner's objections. The new Figures include reference numbers as required by the Examiner specifying the various elements of the invention in Figures 1-3, 4b, and 7-10. Applicants have amended the description of the corresponding Figures in the "Brief Description of the Figures" to reflect the new reference numbers. Applicants have also corrected the typographical errors the specification as directed by the Examiner.

In view of the amendments and the following remarks, Applicants respectfully request reconsideration and reexamination of this application and timely allowance of the pending claims.

I. The Rejection Under 35 U.S.C. § 103(a) Should Be Withdrawn

Claims 1-5, 12-14, 16, 20, 25, 49, and 50 were rejected on pages 4-6 of the Office Action under 35 U.S.C. § 103(a) as allegedly obvious over U.S. Patent No. 6,056,859 to Ramsey *et al.* ("the '859 patent") in view of U.S. Patent No. 6,001,229 to Ramsey *et al.* ("the '229 patent").

Claims 1-5, 12, 13, 15-17, 20-23, 25, and 44-48 were rejected on pages 6-10 of the Office Action under 35 U.S.C. § 103(a) as allegedly obvious over U.S. Patent No. 6,103,537 to Ullman *et al.* ("the '537 patent") in view of JP 11-311616 ("the JP '616 Publication").

Claims 1-13, 15-29, 33-35, and 44-48 were rejected on pages 10-14 of the Office Action under 35 U.S.C. § 103(a) as allegedly obvious over U.S. Reissue No. Re. 36,350 to Swedberg *et al.* ("the '350 Reissue") in view of the JP '616 Publication.

Claims 24 and 26-32 were rejected on pages 14-16 of the Office Action under 35 U.S.C. § 103(a) as allegedly obvious over the '859 patent in view of the '229 patent and in further view of U.S. Patent No. 6,167,910 to Chow *et al.* ("the '910 patent").

Claims 30-32 were rejected on pages 16-17 of the Office Action under 35 U.S.C. § 103(a) as allegedly obvious over the '350 Reissue in view of the JP '616 Publication and in further view of the '910 patent.

Claims 33-43 were rejected on pages 18-20 of the Office Action under 35 U.S.C. § 103(a) as allegedly obvious over the '859 patent in view of the '229 patent and in further view of U.S. Patent No. 6,103,199 to Bjornson *et al.* ("the '199 patent").

Claims 33-43 were rejected on pages 20-22 of the Office Action under 35 U.S.C. § 103(a) as allegedly obvious over the '537 patent in view of the JP '616 Abstract and in further view of the '199 patent.

Applicants respectfully traverse each of these rejections for the reasons set forth herein.

II. The Relevant Case Law

The Federal Circuit has set forth three basic criteria that must be met to establish a case of *prima facia* obviousness. First, there must have been at the time of the invention a motivation to combine or modify the teachings of the references cited. *Ecolochem, Inc. v. Southern California Edison Company*, 227 F.3d 1361, 1372 (Fed. Cir. 2000) (holding obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination); *see also In re Jones*, 958 F.2d 347 (Fed. Cir. 1992); *In re Fine*, 837 F.2d 1071 (Fed. Cir. 1988) (holding that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art). Second, the alleged prior art must teach or suggest all of the limitations of the claims alleged to be obvious. *In re Royka*, 490 F.2d 488 (CCPA 1974) (holding that to establish *prima facia* obviousness of a claimed invention, all of the claim limitations must be taught or suggested by the prior art); *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991) (holding that the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in the applicant's disclosure). Third, there must have been at the time of the invention a reasonable expectation of success. *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1207-

1208 (Fed. Cir. 1991), *cert. denied* 502 U.S. 856 (1991) (holding that obviousness requires references to show that there was, at the time of the invention, a reasonable expectation of success).

III. Applicants Response to the Rejections

A. The Rejection of Claims 1-5, 12, 13, 15-17, 20-23, 25, and 44-48 Under 35 U.S.C. § 103(a) Should be Withdrawn

Claims 1-5, 12-14, 16, 20, 25, 49, and 50 were rejected on pages 4-6 of the Office Action under 35 U.S.C. § 103(a) as allegedly obvious over U.S. Patent No. 6,056,859 to Ramsey *et al.* ("the '859 patent") in view of U.S. Patent No. 6,001,229 to Ramsey *et al.* ("the '229 patent").

According to the Office Action, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the system of the '859 patent to use the electrodes and the electrode controller of the '229 patent because the '859 patent specifically teaches the use of the electrokinetic system of the '229 patent. *See* Office Action at page 6. In particular, it is alleged that the '859 patent discloses a system for separating molecules comprising a microstructure plate, having a plurality of interconnected channels and structures (Fig. 1). *Id.* at page 4. It is further alleged that the structures include a plurality of reservoirs including, a sample accepting section, and electric fields are applied to move the material. *Id.* The structures also include a capture section comprising a capture matrix (DNA probes) affixed to the surface of channel. *Id.* The system is made of a substrate and a sealing (cover) plate that is permanently bonded to the substrate, and one reservoir is held at a lower potential than the other reservoirs. *Id.* Applicants respectfully traverse the rejection for the following reasons.

Applicants respectfully submit that the combination of the '859 patent and the '229 patent fails to teach or suggest the claimed invention. The '859 patent is directed to a method and apparatus for staining immobilized nucleic acids that obviates the need to pre-label the target nucleic acid with a fluorescent, radioactive or other labeling substance. *See* the '859 patent at col. 1, lines 48-51. The '859 patent is further directed to a method and apparatus for staining immobilized nucleic acids that reduces the number of processing steps and the number and type of reagents, thus making the process more economically practical. *Id.* at lines 51-55. According to the specification of the '859 patent, materials are moved through a

microchannel structure by either hydraulic or electrokinetic means. *Id.* at col. 2, lines 54-56. The disclosure states that alternatively materials could be moved by applying electric fields to the material in the reservoirs to impart electroosmotic or electrophoretic movement. *Id.* at lines 59-62.

However, in contrast to the system for separating molecules having different charges and capturing a molecule for detection recited by the pending claims, the '859 patent fails to disclose or even suggest a first electrode microstructure section, a second electrode microstructure section, or a sealing plate layer, which seals at least one channel or microstructure. The '859 patent further fails to disclose or suggest an electrode assembly having at least one first and at least one second electrode, wherein each first electrode microstructure is in electrical contact with at least one first electrode and wherein each second electrode microstructure section in electrical contact with at least one second electrode. In further contrast to the pending claims, the '859 patent does not disclose or suggest a capture microstructure.

The '229 patent fails to remedy the deficiencies of the '859 patent. The '229 patent discloses a microchip apparatus for fluidic manipulations, wherein electrically controlled manipulations of fluids and capillaries in occur micromachine channels. *See* the '229 patent at col. 1, lines 14-15. According to the specification, these manipulations can be used for the electrically controlled manipulation of fluid for capillary electrophoresis, liquid chromatography, and flow injection analysis. *Id* at lines 17-20. Cylindrical plastic reservoirs having open opposite axial ends, are affixed to a base member with portions of the cover plate sandwiched therebetween, with epoxy or other suitable means. *Id.* at col. 4, lines 31-35. Electrical contact is made by placing platinum electrodes in reservoirs. *Id.* at lines 35-37. The electrodes are connected to a power source, which applies a desired potential to select ones of the electrodes. *Id.* at lines 37-40.

The '229 patent does not disclose or suggest a microstructure plate comprising at least one microstructure comprising a series of microstructure sections and channels, wherein each microstructure section is directly interconnected to at least one other microstructure section by at least one channel, the series comprising at least one sample accepting microstructure section, wherein the sample accepting section is fluidly connected to the exterior of the microstructure plate as recited by the pending claims.

As the Examiner is aware, it is the invention as a whole that must be considered in obviousness considerations not bits and pieces of various references. *Hartness International, Inc. v. Simplimatic Engineering Co.*, 819 F.2d 1100 (Fed. Cir. 1987). Neither the '859 patent nor the '229 patent alone or in combination disclose or suggest the claimed invention. In order to contrive a *prima facia* case of obviousness, the combination of the '859 patent and the '229 patent requires one of ordinary skill in the art to impermissibly "pick and choose" the various elements recited by the claims at random from the cited references, which is only possible when using the present claims as a blueprint (*i.e.*, using impermissible hindsight). Applicants respectfully submit that only with the aid of impermissible hindsight could the system for separating molecules having different charges and capturing a molecule of interest for detection as recited by the pending claims be obtained.

For these reasons Applicants respectfully submit that the rejection of claims 1-5, 12, 13, 15-17, 20-23, 25, and 44-48 under 35 U.S.C. § 103(a) should be withdrawn.

B. The Rejection of Claims 1-5, 12, 13, 15-17, 20-23, 25, and 44-48 Under 35 U.S.C. § 103(a) Should be Withdrawn

Claims 1-5, 12, 13, 15-17, 20-23, 25, and 44-48 were rejected on pages 6-10 of the Office Action under 35 U.S.C. § 103(a) as allegedly obvious over U.S. Patent No. 6,103,537 to Ullman *et al.* ("the '537 patent") in view of JP 11-311616 ("the JP '616 Publication").

According to the Office Action, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the plate of the '537 patent to use a sealing plate having openings as taught by the JP '616 Publication because a sealing plate with openings prevents evaporation of the solution within the channels and the openings allow access to the sample inlets and to provide an electrical connection. *See* Office Action at page 9. The Office Action further alleges that it would have been obvious to one having ordinary skill in the art at the time the invention was made to have further modified the electrokinetic means of the '537 patent to use a plurality of electrodes passing through the openings of the plate as taught by the JP '616 Publication because electrodes provide an efficient and controllable means for providing the electrokinetic transport desired in the system the '527 patent. Applicants respectfully traverse the rejection for the reasons set forth below.

The '537 patent discloses methods for conducting a capillary electroseparation

specific binding assays. *See* the '537 patent at col. 3, line 19 to col. 4, line 63. The '537 patent is limited to electroseparation of a labeled first member of a specific binding pair by capillary electroseparation. *Id.* In particular, the '537 patent discloses "methods for masking inhomogeneity of a member of a specific binding pair (sbp) employed in a capillary electroseparation," wherein "the method comprises binding the sbp member to synthetic particles that migrate uniformly or become localized during capillary electroseparation." *Id.* at col. 3, lines 13-17. However, in contrast to the claimed invention, the '537 patent does not disclose or suggest a system for separating molecules as recited by the pending claims. In particular, the '537 patent fails to disclose or suggest a microstructure comprising a series of microstructure sections and channels, wherein each microstructure section is directly interconnected to at least one other microstructure section by at least one channel, the series comprising at least one sample accepting microstructure section, wherein the sample accepting section is fluidly connected to the exterior of the microstructure plate at least one first electrode microstructure section, at least one second electrode microstructure section, at least one capture microstructure section containing a capture matrix, wherein the capture microstructure section is between the first and second electrode microstructure sections in the series wherein the microstructures in the microstructure plate are formed by at least two layers of material, wherein at least one layer is a sealing plate layer which seals at least one channel or microstructure section in the assembled microstructure plate. The '537 patent also fails to disclose or suggest an electrode assembly, the electrode assembly having at least one first and at least one second electrode, wherein each first electrode microstructure section is in electrical contact with at least one first electrode, and wherein each second electrode microstructure section is in electrical contact with at least one second electrode.

The JP '616 Publication fails to remedy the deficiencies of the '537 patent. The JP '616 Publication discloses a "microchip electrophoresis apparatus using the microchip which performs electrophoresis in a separation passage which stuck the transparence plate-like part material of two sheets in more detail, and was formed inside about the electrophoresis apparatus which analyzes the sample of ultralow volume by the high speed and high separation." *See* the JP '616 Publication at ¶ [0001]. The JP '616 Publication does not disclose or suggest a capture microstructure as recited by the pending claims.

Applicants respectfully submit that the Examiner has failed to establish the legally

required *prima facie* case of obviousness based on the disclosures of the '537 patent and the JP '616 Publication. One of ordinary skill in the art would have had not been motivated to combine the teachings of the '537 patent with the disclosure of the JP '616 Publication. Even assuming *arguendo* one of ordinary skill in the art were motivated to make this leap to combine the references, the reference nonetheless fail to recite the claimed invention. In particular, both references fail to disclose the elements recited by the pending claims; thus there is nothing in either disclosure that would motivate one of ordinary skill in the art to include this absent element to obtain the claimed invention.

Applicants respectfully submit that neither the '537 Patent nor the JP '616 Publication alone or in combination disclose or suggest the claimed invention. For these reasons Applicants respectfully submit that the rejection of claims 1-5, 12, 13, 15-17, 20-23, 25, and 44-48 under 35 U.S.C. § 103(a) should be withdrawn.

C. The Rejection of Claims 1-13, 15-29, 33-35, and 44-48 Under 35 U.S.C. § 103(a) Should be Withdrawn

Claims 1-13, 15-29, 33-35, and 44-48 were rejected on pages 10-14 of the Office Action under 35 U.S.C. § 103(a) as allegedly obvious over U.S. Reissue No. Re. 36,350 to Swedberg *et al.* ("the '350 Reissue") in view of the JP '616 Publication.

According to the Office Action, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the electrokinetic means of the '350 Reissue to use any of the electrode assemblies taught by the JP '616 Abstract because each assembly provides an adequate means to provide an electric potential to the solution contained within the microfiuidic channels. *See* Office Action at Page 14. Applicants respectfully traverse the rejection for the reasons set forth below.

The '350 Reissue discloses a miniaturized total analysis system ("μ-TAS") comprising a miniaturized planar column device for use in liquid phase analysis. *See* the '350 Reissue at col. 1, lines 20-21. According to the specification, the μ-TAS includes associated laser-ablated features required for integrated sample analysis, such as analyte detection means and fluid communication means. *Id.* at lines 21-22. The specification discloses that the invention is useful in any analysis system for detecting and analyzing small and/or macromolecular solutes in the liquid phase and may employ chromatographic

separation means, electrophoretic separation means, electrochromatographic separation means, or combinations thereof. *Id.* at Abstract. However, the '350 Reissue fails to disclose a microstructure plate comprising at least one microstructure wherein each microstructure comprises a series of microstructure sections and channels and each microstructure section is directly interconnected to at least one other microstructure section by at least one channel, the series comprising at least one sample accepting microstructure section, wherein the sample accepting section is fluidly connected to the exterior of the microstructure plate; at least one first electrode microstructure section; at least one second electrode microstructure section; at least one capture microstructure section containing a capture matrix, wherein the capture microstructure section is between the first and second electrode microstructure sections as recited by the pending claims.

As set forth above, the JP '616 Publication discloses a "microchip electrophoresis apparatus using the microchip which performs electrophoresis in a separation passage which stuck the transparence plate-like part material of two sheets in more detail, and was formed inside about the electrophoresis apparatus which analyzes the sample of ultralow volume by the high speed and high separation." *See* the JP '616 Publication at ¶ [0001].

Neither the '350 Reissue nor the JP '616 Publication alone or in combination disclose a system for separating molecules having different charges and capturing a molecule of interest for detection as recited by the pending claims. Moreover, even assuming *arguendo* that the cited references independently disclosed the claimed elements, there is no motivation for one of ordinary skill in the art modify the teachings of the '350 Reissue based on the disclosure of the 'JP 616 Publication. As the Examiner correctly points out on page 12 of the Office Action, the '350 Reissue fails to disclose at least one electrode section and at least one second electrode section and an electrode assembly having electrodes associated with each electrode section. However, the legally required motivation to modify the teachings of the '350 Reissue based on the teachings of the JP '616 Publication is absent. Specifically, although the JP '616 Publication discloses the use of an electrode assembly, there is no disclosure or suggestion of the electrode assembly recited by the pending claims, nor is there the suggestion to modify the references.

Thus, neither the '350 Reissue nor the JP '616 Publication alone or in combination disclose or suggest the claimed invention. For these reasons Applicants respectfully submit

that the rejection of claims 1-13, 15-29, 33-35, and 44-48 under 35 U.S.C. § 103(a) should be withdrawn.

D. The Rejections of Claims 24 and 26-32 Under 35 U.S.C. § 103(a) Should be Withdrawn

Claims 24 and 26-32 were rejected on pages 14-16 of the Office Action under 35 U.S.C. § 103(a) as allegedly obvious over the '859 patent in view of the '229 patent and in further view of U.S. Patent No. 6,167,910 to Chow *et al.* ("the '910 patent").

According to the Office Action, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the system described by the '859 patent and the '229 patent to use a three-dimensional arrangement of channels fabricated in a plurality of layers as taught by the '910 patent because the three-dimensional arrangement allows for further reduction in the size of microfluidic devices. *See* Office Action at page 16. It is further alleged that it would have been obvious to one having ordinary skill in the art at the time the invention was made to have modified the polymer material used for the layers in the system described by the '859 patent and the '229 patent to use PDMS or polytetrafluoro-ethylene as taught by the '910 patent because such materials can be easily manufactured at a low cost. *Id.* Applicants respectfully traverse the rejections for the reasons set forth below.

As stated above, the '859 patent is directed to a method and apparatus for staining immobilized nucleic acids that obviates the need to pre-label the target nucleic acid with a fluorescent, radioactive or other labeling substance. *See* the '859 patent at col. 1, lines 48-51. The '859 patent is further directed to a method and apparatus for staining immobilized nucleic acids that reduces the number of processing steps and the number and type of reagents, thus making the process more economically practical. *Id.* at lines 51-55. According to the specification of the '859 patent, materials are moved through a microchannel structure by either hydraulic or electrokinetic means. *Id.* at col. 2, lines 54-56. The disclosure states that alternatively materials could be moved by applying electric fields to the material in the reservoirs to impart electroosmotic or electrophoretic movement. *Id.* at lines 59-62

The '859 patent fails to disclose or even suggest a first electrode microstructure section, a second electrode microstructure section, or a sealing plate layer, which seals at least one channel or microstructure as recited by the pending claims. The '859 patent further fails to disclose or suggest an electrode assembly having at least one first and at least one

second electrode, wherein each first electrode microstructure is in electrical contact with at least one first electrode and wherein each second electrode microstructure section in electrical contact with at least one second electrode.

The '229 patent discloses a microchip apparatus for fluidic manipulations, wherein electrically controlled manipulations of fluids and capillaries in occur micromachine channels. *See* the '229 patent at col. 1, lines 14-15. According to the specification, these manipulations can be used for the electrically controlled manipulation of fluid for capillary electrophoresis, liquid chromatography, and flow injection analysis. *Id* at lines 17-20. Cylindrical plastic reservoirs having open opposite axial ends, are affixed to a base member with portions of the cover plate sandwiched therebetween, with epoxy or other suitable means. *Id.* at col. 4, lines 31-35. Electrical contact is made by placing platinum electrodes in reservoirs. *Id.* at lines 35-37. The electrodes are connected to a power source, which applies a desired potential to select ones of the electrodes. *Id.* at lines 37-40. The '229 patent does not disclose or suggest a microstructure plate comprising at least one microstructure comprising a series of microstructure sections and channels, wherein each microstructure section is directly interconnected to at least one other microstructure section by at least one channel, the series comprising at least one sample accepting microstructure section, wherein the sample accepting section is fluidly connected to the exterior of the microstructure plate as recited by the pending claims.

The '910 patent fails to remedy the deficiencies of the '859 patent and the '229 patent. In particular, the '910 patent discloses multi-layer microfluidic devices and systems (*e.g.*, 3-dimensional). *See* the '910 patent at col. 1, lines 49-51. According to the specification, in one aspect, the invention provides microfluidic devices, which comprise a body structure having at least first, second and third substrate layers, the second substrate layer disposed on top of the first substrate layer and the third substrate layer disposed on top of the second substrate layer. *Id.* at lines 53-57. The specification further discloses that the devices include at least first, second and third ports disposed in the body structure. The devices of the invention also include at least first and second microscale channel networks. The first channel network is typically disposed between the first and second substrate layers, and is in fluid communication with the first and second ports, but not the third port. The second

channel network, on the other hand, is disposed between the second and third layers, and is in fluid communication with the first and third ports, but not the second port. *Id.* at lines 58-67.

The '859 patent, the '229 patent, and the '910 patent taken alone or in combination fail to disclose or suggest the claimed invention. The combination of the '859 patent, the '229 patent, and the '910 patent requires one of ordinary skill in the art to impermissibly "pick and choose" the various elements recited by the claims at random from the cited references, which is only possible when using the present claims as a blueprint (*i.e.*, using impermissible hindsight). The '910 patent is merely directed to a multi-layer microfluidic system that is not related to the pending claims. Thus, one of ordinary skill in the art would not have the legally required motivation to modify the combined teachings of the '859 patent and the '229 patent in view of the '910 patent to render the pending claims obvious. Applicants respectfully submit that only with the aid of impermissible hindsight could the three-dimensional configuration for separating molecules having different charges and capturing a molecule of interest for detection as recited by the pending claims be obtained.

For these reasons Applicants respectfully submit that the rejection of claims 24 and 26-32 under 35 U.S.C. § 103(a) should be withdrawn.

E. The Rejections of Claims 30-32 Under 35 U.S.C. § 103(a) Should be Withdrawn

Claims 30-32 were rejected on pages 16-17 of the Office Action under 35 U.S.C. § 103(a) as allegedly obvious over the '350 Reissue in view of the JP '616 Publication and in further view of the '910 patent.

According to the Office Action, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the polymer material used for the layers in the system described by the '350 Reissue and the JP '616 Abstract to use PDMS or polytetrafluoroethylene as taught by Chow (*i.e.*, the 910 patent) because such materials can be easily manufactured at a low cost. *See* Office Action at page 17.

As stated above, the '350 Reissue discloses a miniaturized total analysis system ("μ-TAS") comprising a miniaturized planar column device for use in liquid phase analysis. *See* the '350 Reissue at col. 1, lines 20-21. According to the specification, the μ-TAS includes associated laser-ablated features required for integrated sample analysis, such as analyte

detection means and fluid communication means. *Id.* at lines 21-22. The specification discloses that the invention is useful in any analysis system for detecting and analyzing small and/or macromolecular solutes in the liquid phase and may employ chromatographic separation means, electrophoretic separation means, electrochromatographic separation means, or combinations thereof. *Id.* at Abstract. The JP '616 Publication discloses a "microchip electrophoresis apparatus using the microchip which performs electrophoresis in a separation passage which stuck the transparence plate-like part material of two sheets in more detail, and was formed inside about the electrophoresis apparatus which analyzes the sample of ultralow volume by the high speed and high separation." *See* the JP '616 Publication at ¶ [0001].

Neither the '350 Reissue nor the JP '616 Publication alone or in combination disclose a system for separating molecules having different charges and capturing a molecule of interest for detection as recited by the pending claims. Moreover, even assuming *arguendo* that the cited references independently disclose the claimed element, there is no motivation for one of ordinary skill in the art modify the teachings of the '350 Reissue based on the disclosure of the 'JP 616 Publication. As the Examiner correctly points out on page 12 of the Office Action, the '350 Reissue fails to disclose at least one electrode section and at least one second electrode section and an electrode assembly having electrodes associated with each electrode section. However, the legally required motivation to modify the teachings of the '350 Reissue based on the teachings of the JP '616 Publication is absent. Specifically, although the JP '616 Publication discloses the use of an electrode assembly, there is no disclosure or suggestion of the electrode assembly recited by the pending claims, nor is there the suggestion to modify the references.

The '910 patent does not remedy the deficiencies of the '350 Reissue and the JP '616 Publication. In particular, the '910 patent discloses multi-layer microfluidic devices and systems (*e.g.*, 3-dimensional). *See* the '910 patent at col. 1, lines 49-51. According to the specification, in one aspect, the invention provides microfluidic devices, which comprise a body structure having at least first, second and third substrate layers, the second substrate layer disposed on top of the first substrate layer and the third substrate layer disposed on top of the second substrate layer. *Id.* at lines 53-57. The specification further discloses that the devices include at least first, second and third ports disposed in the body structure. The

devices of the invention also include at least first and second microscale channel networks. The first channel network is typically disposed between the first and second substrate layers, and is in fluid communication with the first and second ports, but not the third port. The second channel network, on the other hand, is disposed between the second and third layers, and is in fluid communication with the first and third ports, but not the second port. *Id.* at lines 58-67. Although, the '910 patent discloses the substrate materials will comprise polymeric materials, (*e.g.*, plastics, such as polymethylmethacrylate (PMMA) (see the '910 patent at col. 4, lines 40-42), the invention disclosed in the '910 patent is so unrelated to the invention recited by the pending claims that one of ordinary skill in the art would not reasonably be motivated to combine the references.

It follows that because the references fail to render the independent claim obvious they necessarily fail to render a claim from which it depends obvious. For these reasons Applicants respectfully submit that the rejection of claims 24 and 26-32 under 35 U.S.C. § 103(a) should be withdrawn.

F. The Rejections of Claims 33-43 Under 35 U.S.C. § 103(a) Should be Withdrawn

Claims 33-43 were rejected on pages 18-20 of the Office Action under 35 U.S.C. § 103(a) as allegedly obvious over the '859 patent in view of the '229 patent and in further view of U.S. Patent No. 6,103,199 to Bjornson *et al.* ("the '199 patent").\

According to the Office Action, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the channels described in the device of the '859 patent and the '229 patent to use channels with cross-sectional area within the claimed range as taught by the '199 patent because such cross-sectional areas proved for capillary flow. *See* Office Action at page 19. It is further alleged that it would have been obvious to one having ordinary skill in the art at the time the invention was made to have modified the system described by the '859 patent and the '229 patent to use a rectangular 8.5 cm by 11 cm format having an array of 96, 384, or 1536 microstructures as taught by the '199 patent because using a standardized size allows for efficient automation using existing equipment and a plurality of microstructures allows for the simultaneous analysis of many samples at once. *Id.* at page 20.

The '199 patent discloses an apparatus for receiving and dispensing samples such as

in the field of separation of biomolecules and, in particular, separations by capillary electrophoresis and the use of the capillary electrophoresis to detect such biomolecules. *See* the '199 patent at col. 1, lines 6-10. The '199 patent further discloses a plate comprising an array of wells. *Id.* at col. 11, line 40. According to the specification, the plate may have any number of wells, which are usually in a pattern, and are usually 96, 192, 384 or 1536 well plates. Exemplary of such well plates is microtiter plates having a pattern of wells. *Id.* at lines 41-45.

As stated above, the '829 patent fails to disclose or even suggest a first electrode microstructure section, a second electrode microstructure section, or a sealing plate layer, which seals at least one channel or microstructure. The '859 patent further fails to disclose or suggest an electrode assembly having at least one first and at least one second electrode, wherein each first electrode microstructure is in electrical contact with at least one first electrode and wherein each second electrode microstructure section in electrical contact with at least one second electrode. In addition, the '229 patent does not disclose or suggest a microstructure plate comprising at least one microstructure comprising a series of microstructure sections and channels, wherein each microstructure section is directly interconnected to at least one other microstructure section by at least one channel, the series comprising at least one sample accepting microstructure section, wherein the sample accepting section is fluidly connected to the exterior of the microstructure plate as recited by the pending claims.

The '199 patent does not remedy the deficiencies of the combination of the '859 patent and the '229 patent. Although, the '199 patent discloses an array of microstructures, the combination of references fails to recite channels between the microstructure sections of the microstructure having a cross-sectional area between 10,000 and 9,000,000 μm^2.

For these reasons Applicants respectfully submit that the rejection of claims 33-43 under 35 U.S.C. § 103(a) should be withdrawn.

G. The Rejections of Claims 33-43 and 44-48 Under 35 U.S.C. § 103(a) Should be Withdrawn

Claims 33-43 were rejected on pages 20-22 of the Office Action under 35 U.S.C. § 103(a) as allegedly obvious over the '537 patent in view of the JP '616 Abstract and in further view of the '199 patent.

According to the Office Action, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the channels described in the device of the '537 patent and the JP '616 Abstract to use channels with cross-sectional area within the claimed range as taught by the '199 patent because such cross-sectional areas proved for capillary flow. *See* Office Action at page 21-22. It is further alleged that it would have been obvious to one having ordinary skill in the art at the time the invention was made to have modified the system described by the '537 patent and the JP '616 patent to use a rectangular 8.5 cm by 11 cm format having an array of 96, 384, or 1536 microstructures as taught by the '199 patent because using a standardized size allows for efficient automation using existing equipment and a plurality of microstructures allows for the simultaneous analysis of many samples at once. *Id.* at page 22.

The '537 patent discloses methods for conducting a capillary electroseparation specific binding assays. *See* the '537 patent at col. 3, line 19 to col. 4, line 63. The '537 patent is limited to electro-separation of a labeled first member of a specific binding pair. *Id.* In particular, the '537 patent discloses "methods for masking inhomogeneity of a member of a specific binding pair (sbp) employed in a capillary electroseparation," wherein "the method comprises binding the sbp member to synthetic particles that migrate uniformly or become localized during capillary electroseparation." *Id.* at col. 3, lines 13-17. In addition, the '537 patent does not disclose or suggest at least one capture microstructure as recited by the pending claims. The JP '616 Publication discloses a "microchip electrophoresis apparatus using the microchip which performs electrophoresis in a separation passage which stuck the transparence plate-like part material of two sheets in more detail, and was formed inside about the electrophoresis apparatus which analyzes the sample of ultralow volume by the high speed and high separation." *See* the JP '616 Publication at ¶ [0001].

The '199 patent fails to remedy the deficiencies of the '527 patent and the JP '616 Publication. The '199 patent does not remedy the deficiencies of the combination of the '859 patent and the '229 patent. Although, the '199 patent discloses an array of microstructures, the combination of references fails to recite channels between the microstructure sections of the microstructure having a cross-sectional area between 10,000 and 9,000,000 μm^2.

Applicants respectfully submit that the Examiner has failed to establish the legally required *prima facie* case of obviousness based on the disclosures of the '859 patent and the

'229 patent in view of the '199 patent. One of ordinary skill in the art would have had not motivation to combine the teachings of the '859 patent and the '229 patent with the disclosure of the '199 patent. Even assuming *arguendo* one of ordinary skill in the art were motivated to make this leap to combine the references, the reference nonetheless fail to recite the claimed invention. In particular, both references fail to disclose the element P_{Hc2}, thus there is nothing in either disclosure that would motivate one of ordinary skill in the art to include this absent element to obtain the claimed invention.

For these reasons Applicants respectfully submit that the rejection of claims 33-43 under 35 U.S.C. § 103(a) should be withdrawn.

IV. Conclusion

Respectfully, Applicants submit that the rejections to the claims in the application should be withdrawn based on the arguments made herein. Favorable consideration and a Notice of Allowance are earnestly solicited.

Except for issues payable under 37 C.F.R. 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310.

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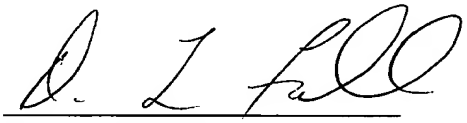

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